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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/365,349	07/30/1999	NORMAN TERRY	B99-085	1676

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EXAMINER

IBRAHIM, MEDINA AHMED

ART UNIT PAPER NUMBER

1638

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/365,349

Applicant(s)

TERRY ET AL

Examiner

Medina A Ibrahim

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 1,2,5-8,13-15,19,20 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3,4,9-12,16-18,21,23 and 24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____. 6) ☐ Other: _____

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114 was filed in this application after a decision by the Board of Patent Appeals and Interferences, but before the filing of a Notice of Appeal to the Court of Appeals for the Federal Circuit or the commencement of a civil action. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10/17/03 has been entered.

2. The decision by the Board of Patent Appeals and Interferences entered on 07/31/03 is summarized as follows:

The rejection of claim 3, under 35 USC 1st paragraph, as being nonenabled was reversed.

The rejection of claims 1-2, 5-8, 13-15, 19-20 and 22 under 35 USC 1st paragraph, as being nonenabled was affirmed.

3. Since the time for appeal of the decision has expired, the affirmance of the rejection of claims 1-2, 5-8, 13-15, 19-20 and 22 for lack of enablement is final. Hence claims 1-2, 5-8, 13-15, 19-20 and 22 are withdrawn from consideration, and must be cancelled in response to this Office action. In canceling these claims, Applicant must ensure that the remaining claims do not depend from a cancelled claim.

Claims 3-4, 9-12, 16-18, 21 and 23-24 are examined in this Office action.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 9-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9 and 12 recite "gene. ...operably linked to a heterologous promoter". A "gene" includes coding, non-coding regions, as well as all regulatory sequences associated with expression. It is unclear whether the heterologous promoter is in addition to the promoter already present in the gene. It is suggested that "gene" be replaced with ---a nucleic acid---.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Brassica plant comprising a recombinant glutamylcyteine synthetase (ECS) expression construct and a method for decreasing heavy metal content of a medium containing an excessive amount of a heavy metal trace element by overexpressing a nucleic acid encoding glutamylcyteine synthetase in said Brassica plant, does not reasonably provide enablement for any Brassicaceae plant species which is genetically engineered to overexpress ECS for enhanced heavy metal accumulation. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), the CAFC considered a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and use the invention. These factors are: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples of the invention; (d) the nature of the invention; (e) the state of the prior art; (f) the predictability or unpredictability of the art; (g) the breadth of the claims; and (h) the relative skill in the art.

The Breadth of the Claim:

The claim is broadly drawn to any plant species from the family of Brassicaceae, which is genetically engineered to overexpress ECS, wherein the transformed plant provides enhanced accumulation of heavy metal as compared with a corresponding wild type plant.

The Amount of Direction or Guidance Presented/The Presence or Absence of Working Examples:

Applicant teaches transformation of *Brassica juncea* with the *E. coli gshI* gene, operably linked to a pea chloroplast transit sequence and to a double 35S CaMV promoter. Applicant teaches analysis of the ECS expression levels in the transgenic lines at the protein level, and growth and tolerance analysis of the transformed seedling/mature plant (EXPERIMENTAL PROTOCOLS AND RESULTS FOR EXEMPLARY

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EMBODIMENTS on pages 8-10). Applicant further teaches analysis of cadmium accumulation and tolerance, and non-protein thiol (NPTS) and glutathione content of the transformed and non-transformed *Brassica juncea* plants. Under Cd treatments, the ECS plants had shown significantly longer shoots and roots than wild type plants. Under control conditions there were no significant differences in root or shoot length between the ECS and the wild type plants. The ECS *Brassica* plants also showed improved Cd accumulation, increased levels of glutathione and non-protein thiol compounds, with no phenotypic differences as compared to untransformed plants (page 11-13).

The specification does not provide sufficient guidance for a plant other than a *Brassica* plant which is genetically engineered to overexpress ECS, and whereby the plant is capable of enhanced heavy metal accumulation as compared to a comparable untransformed plant. While the ECS gene have been isolated and characterized from various organisms, neither the instant specification nor the prior art provides evidence that suggests the overexpression of this enzyme would induce heavy metal accumulation in a nonaccumulator plant.

The specification provides only prophetic guidance for a number of other plant species and their transformation with a number of ECS genes from various organisms for enhanced heavy metal accumulation.

The Nature of the Invention:

Transformation of a plant to overexpress ECS for enhanced heavy metal accumulation is complex. The mechanism of heavy metal accumulation in plants other

than Brassica is yet to be elucidated. See Hofgen et al (Amino Acids (2001) 20:291-299); Salt et al. (Plant Physiology (1996), vol. 109, pp. 1427-1433).

State of the Prior Art/Predictability or Unpredictability of the Art:

The ability of a plant to accumulate heavy metals is a genotype dependent and varies greatly between species and between cultivars within the species (Salt et al Biotechnology, vol. 13, pp. 468-474, 1995). Peer et al. (New phytologist (2003), vol. 159, pp.421-430) teach the use of Brassicaceae plants from the genus of Arabidopsis for phytoremediation. On page 421, 1st full paragraph, Peer states "Arabidopsis thaliana has become a model molecular genetic system for the study of basic plant biology due to its extensive genetic characterization, compact genome, known genomic sequence, compact growth habitat, and the availability of tools for its molecular genetic manipulation. However, it does not accumulate metal". Guerinot et al (Plant Physiology (2001), vol. 125, pp. 164-167) suggest that it is unlikely that the regulation of a single gene will be sufficient to convert non-metal accumulators into metal accumulators.

The state of the prior art as evidenced by Goldsbrough (1999, Applicant's IDS) teaches that overexpression of ECS will not induce enhanced heavy metal accumulation in all Brassicaceae plants. Goldsbrough specifically discloses transformed Arabidopsis plants (Arabidopsis is a genus within the Brassicaceae) that didn't provide increased heavy metal accumulation as compared to control plants. Goldsbrough reports "while ECS could restore some degree of Cd tolerance to a Cd-sensitive mutant (a cad2 mutant having reduced GSH levels), this gene didn't increase Cd tolerance of wild-type plants (page 230, 1st and 2nd full paragraphs).

The *Brassica juncea* is known metal accumulator that has been identified as a plant useful for phytoremediation. In addition, the mechanisms of metal uptake and accumulation in *Brassica juncea* are well documented in the prior art. See, for example, Salt et al. (Plant Physiology (1996), vol. 109, pp. 1427-1433); Raskin et al. (US 5, 785,735); and WO 96/32016)

The Relative Skill in the Art:

The skill of those in the art, who transform plants for overexpression of an enzyme, is high, i.e., generally a PhD in molecular biology/plant physiology.

The Quantity of Experimentation Necessary:

In order for the skilled artisan to carry out the plant and method as claimed, any plant species from Brassicaceae family which is genetically engineered to overexpress ECS, wherein the plant provides enhanced accumulation of heavy metal as compared to a corresponding wild type plant, undue trial and error experimentation would be required. Given the limited guidance in the specification and the uncertain and unpredictable relationship between overexpression of ECS and enhanced heavy metal accumulation of the prior art, undue experimentation would be required to screen through a myriad of transgenic ECS plants of Brassicaceae from varied genera, species and cultivars to identify those with enhanced heavy metal accumulation ability. One skilled in the art would have to proceed with trial and error experimentation to practice the full scope of the claimed invention in view of the lack of guidance in the specification or the prior art. One of skill in the art would not reasonably be able to extrapolate

Applicant's results to non-Brassica plants overexpressing ECS, particularly in view of the negative results with Arabidopsis, absent further guidance.

Therefore, given the breadth of the claims; the lack of guidance; the limited working example; the unpredictability in the art; the state of the art; the level of skill in the art; and the nature of the invention as discussed above, the claimed invention is not enabled throughout the broad scope.

Applicant is invited to provide evidence in the form of a declaration under 37 CFR 1.132 to support broader claim scope. See *In re Budnick*, 537 F.2d 535, 190 USPQ 422 (CCPA, 1976); and *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979).

Double Patenting

8. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

9. Claims 2-4, 9-12, 16-18, 21 and 23-24 rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-23 of prior U.S. Patent No. 6, 576, 816. This is a double patenting rejection.

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 3 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6, 576, 816.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both directed to a transgenic plant of the Brassicaceae family overexpressing ECS for enhanced heavy metal accumulation. The subject matter instantly claimed, which is a Brassicaceae plant genetically engineered to overexpress ECS for enhanced heavy metal accumulation, is anticipated by and therefore obvious over the subject matter claimed in the patent, a Brassica plant comprising a recombinant glutamylcysteine synthetase expression construct for enhanced heavy metal accumulation. The claimed transformed Brassicaceae plant expressing ECS encompasses the transformed Brassica expressing ECS in the patent.

Remarks

12. No claim is allowed.

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Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Medina A. Ibrahim whose telephone number is (571) 272-0797. The Examiner can normally be reached Monday -Thursday from 8:00AM to 5:30PM and every other Friday from 9:00AM to 5:00 PM. Before and After final responses should be directed to fax nos. (703) 872-9306 and (703) 872-9307, respectively.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (571) 272-0804.

4/14/04
mai

A handwritten signature in black ink, appearing to read "Amy Nelson", with a stylized, flowing script.

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
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